Complete Summary

GUIDELINE TITLE

Antithrombotic therapy in patients undergoing percutaneous coronary intervention. In: Sixth ACCP Consensus Conference on Antithrombotic Therapy.

BIBLIOGRAPHIC SOURCE(S)

Popma JJ, Ohman EM, Weitz J, Lincoff AM, Harrington RA, Berger P. Antithrombotic therapy in patients undergoing percutaneous coronary intervention. Chest 2001 Jan;119(1 Suppl):321S-336S. [134 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Conditions, such as coronary artery disease, requiring percutaneous coronary intervention

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To present evidence-based recommendations for the use of antithrombotic therapy in patients undergoing percutaneous coronary intervention for the purpose of reducing ischemic complications and improving patient outcomes

TARGET POPULATION

Patients undergoing percutaneous coronary intervention, including all forms of percutaneous mechanical revascularization, which may involve the use of a single device or multiple new devices and balloons.

INTERVENTIONS AND PRACTICES CONSIDERED

Management/Treatment with Antithrombotic Therapy

1. Oral Antiplatelet Agents:
    - Aspirin therapy
    - Clopidogrel
    - Ticlopidine
    - Aspirin therapy in combination with clopidogrel or ticlopidine

    Note: Dipyridamole is considered but not recommended as an alternative in aspirin-sensitive patients undergoing percutaneous coronary intervention.

2. Platelet Glycoprotein IIb/IIIa Antagonists:
    - Abciximab
    - Eptifibatide
    - Tirofiban
3. Antithrombin Therapy:
    - Heparin
    - Direct Thrombin Inhibitors: Hirudin, bivalirudin

    Note: The following medications are considered but not recommended for prevention of restenosis after coronary angioplasty: unfractionated heparin or low-molecular-weight heparin, platelet thromboxane A_2 and serotonin receptor antagonists, prostacyclin, glycoprotein IIb/IIIa receptor antagonist, omega-3 fatty acid supplements, enoxaparin, r-hirudin, warfarin.

MAJOR OUTCOMES CONSIDERED

Clinical safety and efficacy of treatments, as defined by:

- Relative risk of complications
- Rates of early ischemic complications following percutaneous coronary intervention, such as cardiac death, myocardial infarction, the need for coronary bypass surgery, repeat angioplasty, target lesion revascularization, angiographic thrombosis
- Rates of adverse effects from treatment, such as bleeding

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The participants reviewed information from an exhaustive review of the literature.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) (see "Rating Scheme for the Strength of the Recommendations") and the methodologic quality of the underlying evidence (A, B, C+, or C).

Grades of evidence for antithrombotic agents:

1A
Methodological strength of supporting evidence: randomized controlled trials without important limitations

1B
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)

1C+
Methodological strength of supporting evidence: no randomized controlled trials, but randomized controlled trial results can be unequivocally extrapolated; or, overwhelming evidence from observational studies

1C
Methodological strength of supporting evidence: observation studies

2A
Methodological strength of supporting evidence: randomized controlled trials without important limitations

2B
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)

2C
Methodological strength of supporting evidence: observational studies

* Such situations include randomized controlled trials with lack of blinding, and subjective outcomes, in which the risk of bias in measurement of outcomes is high; and randomized controlled trials with large loss to follow-up.

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Observational Trials
Meta-Analysis of Randomized Controlled Trials
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The strength of any recommendation depends on two factors: the trade-off between benefits and risks, and the strength of the methodology that leads to estimates of the treatment effect. The rating scheme used for this guideline captures these factors. The guideline developers grade the trade-off between benefits and risks in two categories: (1) the trade-off is clear enough that most patients, despite differences in values, would make the same choice; and (2) the trade-off is less clear, and each patient's values will likely lead to different choices.

When randomized trials provide precise estimates suggesting large treatment effects, and risks and costs of therapy are small, treatment for average patients with compatible values and preferences can be confidently recommended.

If the balance between benefits and risks is uncertain, methodologically rigorous studies providing grade A evidence and recommendations may still be weak (grade 2). Uncertainty may come from less precise estimates of benefit, harm, or costs, or from small effect sizes.

There is an independent impact of validity/consistency and the balance of positive and negative impacts of treatment on the strength of recommendations. In situations when there is doubt about the value of the trade-off, any recommendation will be weaker, moving from grade 1 to grade 2.

Grade 1 recommendations can only be made when there are precise estimates of both benefit and harm, and the balance between the two clearly favors recommending or not recommending the intervention for the average patient with compatible values and preferences. Table 2 of the original guideline document summarizes how a number of factors can reduce the strength of a recommendation, moving it from grade 1 to grade 2. Uncertainty about a recommendation to treat may be introduced if the target event that is trying to be prevented is less important (confident recommendations are more likely to be made to prevent death or stroke than asymptomatic deep venous thrombosis); if the magnitude of risk reduction in the overall group is small; if the risk is low in a particular subgroup of patients; if the estimate of the treatment effect, reflected in a wide confidence interval (CI) around the effect, is imprecise; if there is substantial potential harm associated with therapy; or if there is an expectation for a wide divergence in values even among average or typical patients. Higher costs would also lead to weaker recommendations to treat.

The more balanced the trade-off between benefits and risks, the greater the influence of individual patient values in decision making. If they understand the benefits and risks, virtually all patients will take aspirin after myocardial infarction or will comply with prophylaxis to reduce thromboembolism after hip replacement. Thus, one way of thinking about a grade 1 recommendation is that variability in patient values or individual physician values is unlikely to influence treatment choice in average or typical patients.

When the trade-off between benefits and risks is less clear, individual patient values will influence treatment decisions even among patients with average or typical preferences.

Grade 2 recommendations are those in which variation in patient values or individual physician values will often mandate different treatment choices, even among average or typical patients.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodologic quality of the underlying evidence (A, B, C+, or C) (see "Rating Scheme for the Strength of the Evidence").

Grades of recommendation for antithrombotic agents:

1A
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; can apply to most circumstances, without reservation

1B
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; likely to apply to most patients

1C+
Clarity of risk/benefit: risk/benefit clear

Implications: strong recommendation; can apply to most patients in most circumstances

1C
Clarity of risk/benefit: risk/benefit clear
Implications: intermediate-strength recommendation; may change when stronger evidence available

2A
Clarity of risk/benefit: risk/benefit unclear
Implications: intermediate strength recommendation; best action may differ, depending on circumstances or patients' societal values

2B
Clarity of risk/benefit: risk/benefit unclear
Implications: weak recommendation; alternative approaches likely to be better for some patients under some circumstances

2C
Clarity of risk/benefit: risk/benefit unclear
Implications: very weak recommendation; other alternatives may be equally reasonable

COST ANALYSIS

While the American College of Chest Physicians conference participants considered cost in deciding on the strength of recommendations, the paucity of rigorous cost-effective analyses and the wide variability of costs across jurisdictions led the guideline developers to take a conservative approach to cost issues. That is, cost considerations influenced the recommendations and the grades of those recommendations only when the gradient between alternatives was very large.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The initial guidelines were prepared by the chapter committee (the primary authors) and then reviewed separately by the Committee Co-Chairs and methodology experts and finally by the entire group of Consensus Guideline participants.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Please note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary. The recommendations that follow are based on the previous version of the guideline.

Excerpted by the National Guideline Clearinghouse (NGC):

The grading scheme is defined at the end of the Major Recommendations.

Oral Antiplatelet Agents

1. The guideline developers recommend pretreatment with aspirin to reduce the incidence of early complications after percutaneous coronary intervention (grade 1A). The recommended dose for aspirin is 80 to 325 mg (grade 2A).
2. The guideline developers recommend long-term aspirin therapy (80 to 325 mg daily) for secondary prevention of cardiovascular events (grade 1A). There is no convincing evidence that long-term aspirin therapy influences the rate of restenosis after percutaneous coronary intervention.
3. For patients undergoing balloon angioplasty or atherectomy alone who cannot tolerate aspirin, the guideline developers recommend pretreatment with clopidogrel, 300 mg oral loading dose and 75 mg daily before the procedure (grade 2A), or ticlopidine, 500 mg loading dose and 250 mg twice daily before the procedure (grade 2A). Ticlopidine has important side effects.
4. The guideline developers recommend that clinicians not use dipyridamole as an alternative in aspirin-sensitive patients undergoing percutaneous coronary intervention (grade 2A).
5. As an adjunct to aspirin therapy in patients undergoing stent implantation, the guideline developers recommend treatment with clopidogrel, 300 mg oral loading dose and 75 mg daily for 14 to 30 days (grade 2A), or ticlopidine, 500 mg loading dose and 250 mg twice daily for at least 10 to 14 days after the procedure (grade 2A). Ticlopidine has important side effects.

Platelet Glycoprotein IIb/IIIa Antagonists

1. The guideline developers recommend that glycoprotein IIb/IIIa receptor inhibition using abciximab, eptifibatide, or tirofiban be considered in all patients undergoing percutaneous coronary interventions, particularly those patients who have refractory unstable angina or other high-risk features (grade 1A).
2. The guideline developers recommend that abciximab is considered in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction to reduce ischemic complications (grade 2A).

Antithrombin Therapy

Heparin

1. The guideline developers recommend administration of unfractionated heparin to achieve an activated clotting time of 250 to 300 seconds with the HemoTec device and 300 to 350 seconds with the Hemochron device. Weight-adjusted heparin boluses (60 to 100 International Units per kilogram) can be used to avoid excessive levels of anticoagulation (all grade 1C).
2. The guideline developers do not recommend routine postprocedural infusion of heparin in patients with uncomplicated procedures (grade 1C).
3. The guideline developers recommend early sheath removal when the activated clotting time falls to less than 150 to 180 seconds to reduce the incidence of complications at the access site (grade 1C).

4. When abciximab therapy is used, the heparin bolus should be reduced to 50 to 70 International Units per kilogram to achieve a target activated clotting time of greater than 200 seconds with either the HemoTec or Hemochron device. Femoral sheaths should be removed after the procedure as when the activated clotting time falls to less than 150 to 180 seconds (grade 1A).

Direct Thrombin Inhibitors

1. The guideline developers recommend that bivalirudin may be given as an alternative to heparin in patients undergoing percutaneous coronary interventions (grade 2A).
2. The guideline developers recommend that direct thrombin inhibitors be used as alternative anticoagulants to unfractionated heparin in patients with known or suspected heparin-induced thrombocytopenia (grade 2A).

Antithrombotic Agents To Prevent Restenosis After Coronary Angioplasty

1. The guideline developers do not recommend the prolonged use of postprocedural low-dose unfractionated heparin (grade 1C) or low-molecular-weight heparin in patients undergoing uncomplicated percutaneous coronary interventions for the prevention of restenosis (grade 1A).

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodologic quality of the underlying evidence (A, B, C+, or C).

Definitions:

Grades of recommendations:

1A

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: randomized controlled trials without important limitations
Implications: strong recommendation; can apply to most circumstances, without reservation

1B

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)
Implications: strong recommendation; likely to apply to most patients

1C+

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: no randomized controlled trials, but randomized controlled trial results can be unequivocally extrapolated; or, overwhelming evidence from observational studies

Implications: strong recommendation; can apply to most patients in most circumstances

1C

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: observation studies
Implications: intermediate-strength recommendation; may change when stronger evidence available

2A

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: randomized controlled trials without important limitations
Implications: intermediate strength recommendation; best action may differ, depending on circumstances or patients' societal values

2B

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)
Implications: weak recommendation; alternative approaches likely to be better for some patients under some circumstances

2C

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: observational studies
Implications: very weak recommendation; other alternatives may be equally reasonable

* Such situations include randomized controlled trials with lack of blinding, and subjective outcomes, in which the risk of bias in measurement of outcomes is high; and randomized controlled trials with large loss to follow-up.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified for each recommendation (refer to "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate antithrombotic therapy in patients undergoing percutaneous coronary intervention may reduce the relative risk and actual incidence of ischemic complications (such as cardiac death, myocardial infarction, the need revascularization, angiographic thrombosis), as well as reduce the risk for complications of therapy, such as major bleeding.

Conventional antithrombotic strategies have not consistently reduced the frequency of angiographic or clinical restenosis after coronary angioplasty.

Several tables in the original guideline document summarize the results (procedural and patient outcomes) of trials on various antithrombotic therapies in patients undergoing percutaneous coronary interventions.

POTENTIAL HARMS

The primary risk of antithrombotic therapy is bleeding.

Potential side effects of the following medications are specifically identified:

- Ticlopidine. Side effects of ticlopidine, an oral antiplatelet agent, may include gastrointestinal symptoms, cutaneous rashes, and biochemical abnormalities in liver function tests. However, the major side effect is severe leukopenia (granulocyte count, less than 450/microliter), which can occur in up to 1% of patients. In most cases, the neutropenia is reversible after the discontinuation of ticlopidine therapy, but episodes of sepsis and death have occurred. Serious and fatal episodes of thrombotic thrombocytopenic purpura also have been reported. A shorter duration (10 to 14 days) of ticlopidine therapy may reduce the risk of these side effects.
- Clopidogrel. Rare hematologic complications, including hemolytic-uremic syndrome and thrombotic thrombocytopenic purpura have also been reported with clopidogrel use.
- Abciximab. One limitation of abciximab use is the development of human antichimeric antibodies in 3 to 5% of patients, which may potentially preclude readministration. In one registry, 92 patients with prior exposure to abciximab were retreated with abciximab. Acute thrombocytopenia (platelet count, less than 100,000/mL) occurred in 6.5% of patients, and severe thrombocytopenia (platelet count, less than 50,000/mL) developed in 2.2% of patients. No patient developed profound thrombocytopenia (platelet count, less than 20,000/mL), and there were no episodes of death, intracranial bleeding, or allergic reactions with abciximab readministration.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Interpreting the Recommendations

The authors of these guidelines offer recommendations that should not be construed as dictates by the readers, including clinicians, third-party payers, institutional review committees, and courts. In general, anything other than a 1A recommendation indicates that the chapter authors acknowledge that other interpretations of the evidence and other clinical policies may be reasonable and appropriate. Even grade 1A recommendations will not apply to all circumstances and all patients. For instance, the guideline developers have been conservative in their considerations of cost, and have seldom downgraded recommendations from 1 to 2 on the basis of expense. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far more than some of the interventions that the developers designate grade 1A. This will likely be true for all less-industrialized countries. However, a weak recommendation (2C) that reduces resource consumption may be more strongly indicated in less-industrialized countries.

Similarly, following grade 1A recommendations will at times not serve the best interests of patients with atypical values or preferences. For instance, consider patients who find anticoagulant therapy extremely aversive, either because it interferes with their lifestyle (prevents participation in contact sports, for instance) or because of the need for monitoring. For such patients, clinicians may reasonably conclude that following some grade 1A recommendations for anticoagulation will be a mistake. The same may be true for patients with particular comorbidities (such as a recent GI bleed or a balance disorder with repeated falls) or other special circumstances (such as very advanced age).

The guideline developers trust that these observations convey their acknowledgment that no guidelines or recommendations can take into account the often compelling idiosyncrasies of individual clinical circumstances. No clinician and no one charged with evaluating the actions of a clinician should attempt to apply.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Popma JJ, Ohman EM, Weitz J, Lincoff AM, Harrington RA, Berger P. Antithrombotic therapy in patients undergoing percutaneous coronary intervention. Chest 2001 Jan;119(1 Suppl):321S-336S. [134 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

Funding was supplied by DuPont Pharmaceuticals.

GUIDELINE COMMITTEE

American College of Chest Physicians Consensus Panel on Antithrombotic Therapy

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

Please note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

GUIDELINE AVAILABILITY

Electronic copies of the updated guideline: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Sixth ACCP Consensus Conference on Antithrombotic Therapy (2001): quick reference guide for clinicians. Northbrook, IL: ACCP, 2001.

Electronic copies: Available in from the American College of Chest Physicians Web site. (Downloadable files intended for use with Palm OS compatible devices are available.)

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348, or by calling 1 (800) 343-2227.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on July 30, 2001. The information was verified by the guideline developer on October 31, 2001.

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